

Fresh Frozen Plasma Transfusion Induced Anaphylactic Shock: A Case Report

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Abstract

Introduction: The adverse transfusion reactions (ATRs) underlying the developments of transfusion severely disturbed transfusion therapy, which should deserve more attention from technologists.

Case Presentation: One bag of Fresh Frozen Plasma (FFP) was implicated in one case of anaphylactic shock in a pediatric rhabdomyosarcoma (RMS) patient. The plasma from a donor and the pre-/post-transfused plasma from the patient was used to evaluate the immunoglobulin (Ig) A, IgE by serum immunoglobulin assay, and interleukin (IL) 2, IL-4, IL-6, IL-10, TNF and IFN- γ by flow cytometry. The IgE concentration in the plasma from the pre-transfused patient was 1980 IU/mL, which indicates that the patient was in a hyperallergenic state prior to FFP transfusion, and with a history of anaphylactic reaction induced by plasma transfusion and that coupled with continuous stimulation of plasma components induced the occurrence of anaphylactic shock. The IgE level increased to 3160 IU/mL when the shock occurred. The IL-6 and IL-10 were elevated from 218.7 pg/mL before transfusion to 284.1 pg/mL after transfusion and from 4.2 pg/mL to 15.8 pg/mL.

Conclusions: The high concentration of IgE in the patient with a history of allergy before transfusion can induce severe ATRs, leading to the occurrence of anaphylactic shock, and although rare, it should not be ignored. These patients need management that is more advanced and examinations before plasma transfusion and more inspections during the transfusion process.

Keywords: Fresh Frozen Plasma, Anaphylactic Shock, IgE

1. Introduction

Fresh Frozen Plasma (FFP) transfusion is mainly indicated for the deficiency of clotting factors with abnormal coagulation tests in the presence of active bleeding or the alternative treatment strategy used to prevent clinical bleeding and blood oozing, especially in perioperative period due to the deficiency of multiple clotting factors or the reversal of warfarin in the presence of active bleeding [1,2]. The FFP contains many clotting factors so that the coagulation condition can be improved immediately. However, FFP also contains the amount of albumin and other polymorphic serum proteins (e.g., haptoglobin, transferrin and others), and protease inhibitors, these heterologous proteins, as allergens, have proved the relations between allergic reactions from mild to

anaphylactoid [3,4]. These allergens react with the IgE antibody bound to basophils or mast cells in the recipient's blood, these cells' granule contents are then released, and these, together with prostaglandin and leukotriene mediators produced promptly by the same cells, act on a variety of target tissues to cause immediate physiologic reactions [5]. When the same antigenic substance is exposed to the sensitized body again, it can trigger a broad type I allergic reaction.

Anaphylactic shock belongs to allergic transfusion reactions (ATR), a rare but severe allergic reaction that can induce death. It is most often caused by an allergy to food, certain medications, or blood transfusion [6]. In 1984, Sabet W. Hashim reported that

nine episodes of fulminant noncardiogenic pulmonary oedema after cardiopulmonary bypass were observed in eight patients between September 1977 and December 1982, and which finally was certified that was most probably anaphylactic reactions to FFP [7]. In China, in two studies of plasma exchange in the treatment of severe hepatitis, the proportion of reported cases of anaphylactic shock was 1.09% and 0.48%, respectively [8]. The FFP in this report was accepted by undergoing polymerase chain reaction nucleic acids testing for HIV, HBV, and HCV to reduce the risk of transfusion-transmitted infections.

2. Case Report

A 4-year-old pediatric patient was admitted to the Oncology Surgery in our hospital on May 11, 2022, after being diagnosed with Rhabdo Myo Sarcoma (RMS) for more than one year. Before this visit, the patient had received the tumour biopsy to confirm the RMS diagnosis and four rounds of chemotherapy. The massive pelvic tumour resection surgery was performed on May 28, 2021. Following this surgery, long-term chemotherapy treatments were administered from May 28, 2021, to Sep 2, 2021. One metastatic mass (33*23 mm) was detected by positron emission tomography CT (PET-CT) to consider RMS relapse on Sep 26, 2021. Following admission on May 11, 2022, the pertinent tests were finished, and contraindications were ruled out. On May 12, 200 mL RBCs were transfused for a lower haemoglobin level. On May 18, laparotomy was performed while the patient was under general anaesthesia for the removal of the left retroperitoneal tumor, the dissection of the retroperitoneal lymph nodes, the removal of the left ureter, the creation of the left pyelostomy, and the release of the intestinal adhesions. During the surgery, 400 mL of red blood cells (RBCs) and 150 mL of FFP were transfused, and there were no apparent ATRs. The patient was still under anaesthesia and receiving support from a ventilator in the intensive care unit (ICU), with blood pressure 100/46 mmHg, heart rate 115 bpm and SpO2 100%.

On May 19, weaning the machine off was completed without incident. Following that, because of the blood oozing, the Haemoglobin (Hb) and hematocrit (Hct) dropped to 69 g/L and 21.5%, respectively. As a result, one unit of the group (A) Rh (D) positive RBCs was transfused at 09:34 without ATRs. At 12:08, 120 mL of the group (A) Rh (D) FFP began to transfuse and completed transfusion at 13:33 on account of poor coagulation function, meanwhile, the patient presented with wheal-like rash and decreased blood pressure, those symptoms were relieved after the treated with ankylodnisolone, epinephrine, saline and isopromazine. Worse still, anaphylactic shock occurred at 13:50, namely 17 minutes after the completion of the FFP transfusion, with blood pressure 78/40 mmHg, and heart rate 130 bpm. Following that, the lateral thigh muscle was intramuscularly injected with 0.15 mg of adrenaline, saline expansion, and Phenergan given was performed. After the above anti-shock treatment, the blood pressure and heart rate recovered to 104/67 mmHg and 98 bpm, respectively, and the rash had subsided compared to before. The timeline of the medical history of this time anaphylactic shock shown in Figure 1.

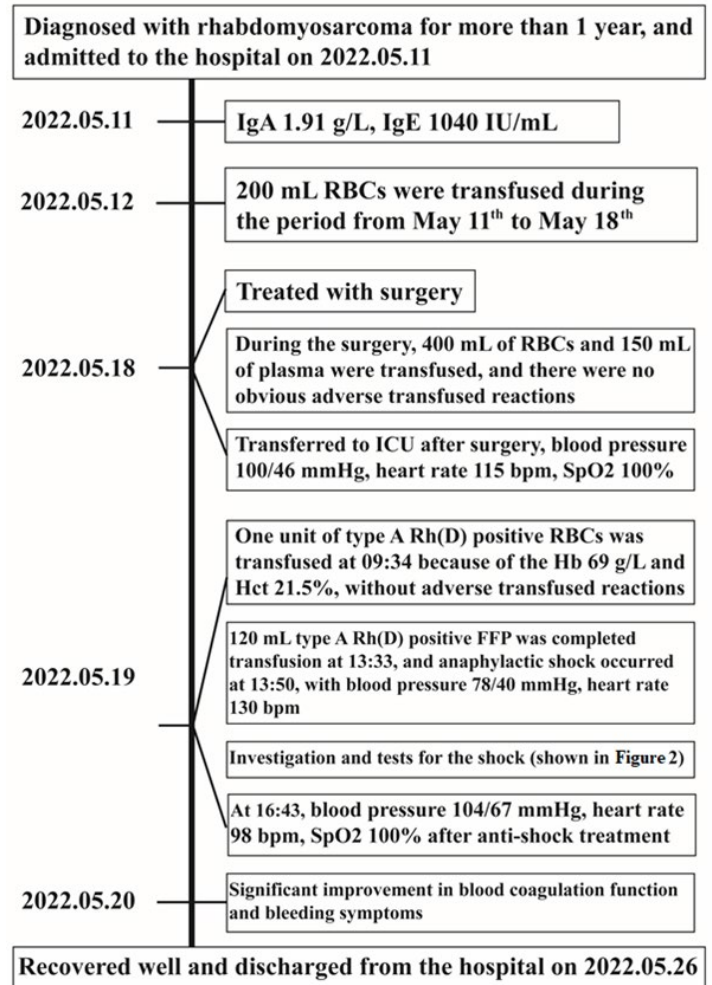


Figure 1: The Timeline of the Medical History of this Time Anaphylactic Shock

We reviewed the medical records and found that the patient had a history of allergy induced by platelets transfusion. The IgE had reached 1040 IU/mL in the admission examinations. Then, we collected the venous blood before and after the FFP transfusion and the blood from the donor. Following that, there were no exceptions when we reperformed the crossmatching test. The IgA and IgE in the plasma from the donor and the pre-/post-transfused plasma from the patient were evaluated by serum immunoglobulin assay (IgA, 7180 automatic biochemical analyzer, Reagent Lot No.1898993, Hitachi, Japan; IgE, BNII System, Reagent Lot No.169601, Siemens, Germany), and IL 2, IL-4, IL-6, IL-10, TNF and IFN- γ by flow cytometry (BD FACSCaliburTM Flow Cytometer, Multiplex Cytokine Assay Kits, Lot No. 20220901, Biosciences, USA). The data in Figure 2 showed that the patient had already been hyperallergenic with the IgE 1980 IU/mL; the anaphylactic condition persisted until after the FFP transfusion (IgE 3160 IU/mL). We also found that the IL-6 in pre-transfused serum had been seriously elevated to 218.7 pg/mL. Namely, the patient was in a state of inflammation and immune activation, and the concentration increased to more than 284.1 pg/mL after the FFP

transfusion with the continuous inflammation status. Meanwhile, the level of IL-10 in post-transfusion was increased compared with that in pre-transfusion (15.8 vs 4.2 pg/mL), which may illustrate

the hypotension state, and participated in the anti-inflammatory and anti-allergic reactions with IL-6 and the other cytokines.

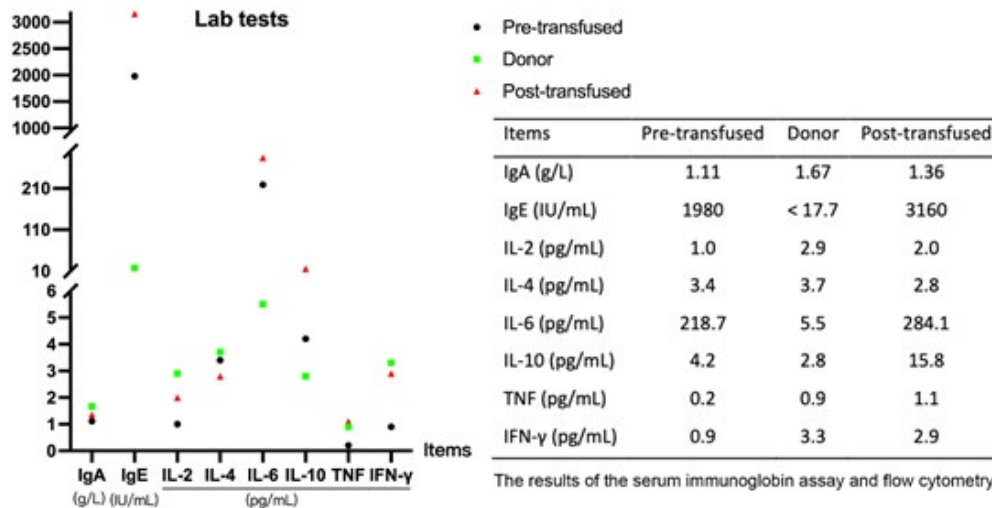


Figure 2: The Lab Tests for IgA, IgE, IL-2, IL-4, IL-6, IL-10, TNF and IFN-γ, in the Serum from the Pre-/Post-Transfused Patient and the Donor

The day after the treatment of the FFP transfusion, May 20, 2022, the patient had no rash or shock symptoms, and the coagulation function and bleeding symptoms improved significantly. The above results suggested that the function of FFP transfusion was practical but without better security. In addition, on the same day, the patient was transferred to the general ward from the ICU. In the surgical oncology ward, symptomatic and supportive treatments were performed, including intravenous hypertrophic nutrition support therapy, anti-infection, nebulized phlegm, and liver protection. After a few days of treatment, the patient's inflammatory indicators decreased significantly. Some other discomfort symptoms were relieved, and finally, this pediatric patient was discharged from our institution on May 26, 2022.

3. Discussion

Although allergic reactions occur most frequently, life-threatening anaphylaxis rarely occurs in 1:20 000~50 000 transfusions [9]. The occurrence of the ATRs depends on two major pathways, the allergen-dependent and allergen-independent [10].

The Former Included:

- 1) Plasma Proteins as Allergens (Eg: IgA- and Haptoglobin-Deficient)
- 2) Chemical Allergens (Eg: methylene blue)
- 3) Food Allergens
- 4) Histamine-Mediated Pathway and Platelet-Activating Factor (Paf)-Mediated Pathway

The Latter Included:

- 1) Diseases (Eg: chronic idiopathic Urticaria)
- 2) Passive Transfer of IgG or IgM Antibodies (Eg: Anti-IgA from Donors)

3) Passive Sensitization (Significant Levels of IgE Antibodies to Common Allergens) [10].

Rachid R et al. reported that patients who suffer from plasma allergy have been shown to have low levels of IgA in their serum (IgA levels lower than 50 mg/L) [11]. IgA-deficient patients are more likely to generate specific antibodies, which can lead to anti-IgA-mediated transfusion reactions when blood components containing IgA transfused into these patients. The proportion of IgA-deficient patients in the population of China is about 1/5000~1/1615 [12]. The serum IgA concentration of the patient in this report was 1.11 g/L (or 111 mg/dL), namely that this patient was not IgA-deficient.

As we all know that most cases of anaphylactic shock are IgE-mediated, and a variety of chemical mediators are released, including histamine, heparin, tryptase, PAF, bradykinin, tumour necrosis factor, nitrous oxide, and several types of interleukins [13]. After further research in this report, we found that the patient's serum IgE level had previously been high before receiving the FFP transfusion (1980 IU/mL), indicating the patient was already in an allergic status. In addition, before this hospitalization, the patient had a history of plasma-induced allergy. When the plasma transfused again, the patient went into anaphylactic shock because of the previous activation of the patient's immune system brought on by the blood transfusion during the procedure, and the IgE level increased to 3160 IU/mL. In summary, we concluded that the IgE level in the patient increased from 1040 IU/mL on admission to 1980 IU/mL after surgical transfusion and then to 3160 IU/mL after FFP transfusion following surgery, the continuous stimulation of plasma components led to the development of anaphylactic shock. In addition, the level of IL-6 and IL-10 increased from 218.7 pg/mL and 4.2 pg/mL to 284.1 pg/mL and 15.8 pg/mL

after FFP transfusion, and those were involved in the progress of anaphylactic shock.

In one meta-analysis, Wang Y et al. demonstrated that children transfused with RBCs and platelet products exhibited a higher adverse reaction incidence than adults and no significant differences in plasma. Meanwhile, the authors also reported that the incidence of allergic reactions was significantly higher in children than in adults (RR = 2.98, 95% CI: 1.78–4.98; $p < .0001$) [14]. Yanagisawa et al. announced that anaphylaxis occurred shortly after transfusion compared with minor ATRs, which were similar to that in adults [15]. In general, the start of anaphylaxis caused by numerous triggers in children and adults can occur over a wide range of times, from minutes to hours following exposure to a trigger. Children, especially infants and young children, because they cannot express themselves well, and skin symptoms may

not be easy to detect in time. Nurses or surgeons must strengthen the inspections during blood transfusion, especially those with a history of transfusion allergy.

4. Conclusion

In conclusion, before transfusing plasma products, the physicians should thoroughly inquire about the patient's medications history and allergy history, especially with/without a history of plasma-induced allergy. Then, laboratory tests must be completed, including antibody testing on IgA and IgE, even tryptase test, mast cell mediators' measurement and basophil activation test (BAT). The physicians and surgeons can perform more management that is advanced and examinations before plasma transfusion and more inspections during the transfusion process, as illustrated in Figure 3.

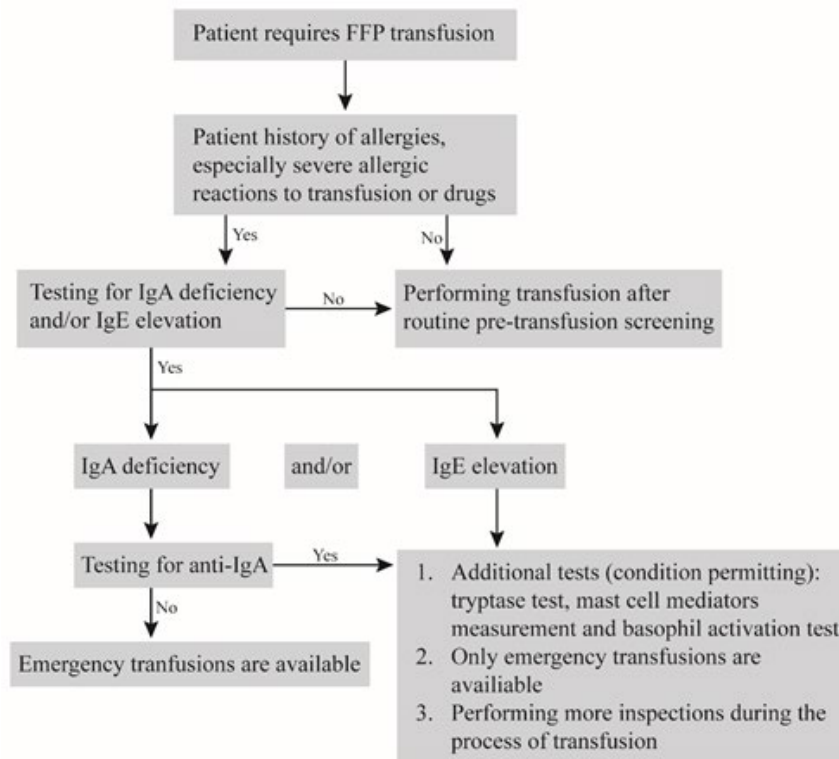


Figure 3: Clinical Decision-Making Algorithm for IgE, IgA, and Anti-IgA Testing in Patients Requiring FFP Transfusion

Declarations

Ethics Approval

This was a retrospective analysis of residual specimens, all usage data were anonymous, the requirement for informed consent was waived, and the study was conducted following the Declaration of Helsinki and with approval from the Ethics Committee of Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health (Approval Number 2023-IRB-0026).

Consent to Participate

Informed consent was obtained from the patient and the legal guardians.

Written Consent for Publication

The patient and the family have consented to submitting the case data to the journal.

Availability of Data and Material

The datasets used and analyzed during the present study are available from the corresponding author upon reasonable request.

Author Contributions

Ming-Wei Yin conceived, designed the study, and drafted the manuscript. Ji-Hua Ma collected the clinical data. Gui-Zhen Jiang and Ning Zhao performed the immunoglobulin and flow cytometry tests. Ming-Wei Yin and Ji-Hua Ma participated in the serological study and analysis of the data. Xue-Jun Chen revised the manuscript. All authors contributed to the article and approved the submitted version.

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